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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
HOLLERAN, A	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/229,229	Wahl et al
Examiner	**Group Art Unit**
Anne Holleran	1642

☒ Responsive to communication(s) filed on *Jan 5, 2001*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-32* is/are pending in the applicat

Of the above, claim(s) *5-27, 31, and 32* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4 and 28-30* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

1. This Office Action is responsive to the Amendment filed January 5, 2001.

New claims, numbered as 5-9, were added. However, claims 5-9 already exist. Therefore, under 37 CFR 1.126, the claims were renumbered as 28-32. Additionally, it is noted that the amendment contained directions to add new claims 5-11. To clarify the record, only new claims labeled 5-9 were presented.

Election/Restriction:

2. New claims 31 and 32 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Amended claims 31 and 32 are directed to methods for in vivo testing, classified in class 424 and subclass 9.1, for example. Thus, new claims 31 and 32 are drawn to an art recognized different class of invention than the originally elected claims 1-4 which were drawn to in vitro methods of identifying therapeutic agents, classified in class 435 and subclass 4. In vivo methods of testing are separate and distinct methods requiring different searches of the U.S. Patent shoes and the non-patent literature.

Since Applicant has received an Action on the Merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 31 and 32 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-32 are pending.

Claims 5-27, 31 and 32, drawn to non-elected inventions, are withdrawn from consideration.

Claims 1-4 and 28-30 are examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

4. The rejection of Claims 1-4 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying agents which induce reduction or elimination of DM or extrachromosomal DNA by measuring micronuclei formation, does not reasonably provide enablement for making and using methods for identification of therapeutic agents which induce cell maturation or cell death by measuring levels of DM or extrachromosomal DNA is withdrawn in light of the amendment to the claims.

5. The rejection of claims 1 and 4 under 35 U.S.C. 102(b) as being anticipated by Tometsko (U.S. Patent 5,229,265; published Jul. 20, 1993) is withdrawn in view of the amendment.

6. The rejection of claims 1 and 4 under 35 U.S.C. 102(e) as being anticipated by Dertinger et al (U.S. Patent 5,858,667; published Jan. 12, 1999; filed Sep. 6, 1996) is withdrawn in view of the amendment.

Claim Rejections Maintained:

7. The rejection of claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

The amendments to claim 1 have not provided a correlative recitation to relate increased levels of micronucleation with a decrease in the presence of double minute chromosomes or extrachromosomal DNA.

New Grounds of Rejection:

8. Claims 28 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 28 and 30 are vague and indefinite because it is not clear what biological process "reversion" refers to. If Applicant intends "reversion of the neoplastic phenotype" then claims 5, 7 and 9 should be amended accordingly.

Claims 28 and 30 are vague and indefinite. Each of these claims should be rewritten as independent claims because each of these claims changes the endpoint of the assay step as recited in the independent claims from which claims 28 and 30 depend. For example, in claim 1 the assay step determines the level of micronucleation of double minute chromosomes or extrachromosomal DNA, whereas in dependent claim 28, the assay step determines whether the treated test cells

have undergone reversion, differentiation or apoptosis. Thus, dependent claim 28 does not contain all of the limitations of claim 1, from which it depends.

9. Claims 1, 3, 28, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckhardt et al (Eckhardt, S.G. et al, Proc. Natl. Acad. Sci. USA, 91: 6674-6678, 1994; cited in the IDS) in view of Snapka et al (Snapka, R.M. et al, Proc. Natl. Acad. Sci., USA, 80: 7533-7537, 1983; cited in the IDS).

Claim 1 is drawn to a method of identifying a therapeutic agent which decreases the presence of double minute chromosomes or extrachromosomal DNA in a cell comprising assaying treated cells to determine their level of micronucleation of double minute chromosomes or extrachromosomal DNA. It is assumed that the increased micronucleation leads to a decrease in the presence of double minute chromosomes or extrachromosomal DNA. Claim 28 is drawn to a method of identifying a therapeutic agent comprising assaying treated cells to determine whether they have undergone reversion, differentiation or apoptosis. Claim 29 is drawn to a method of identifying a therapeutic agent suitable for treatment of neoplastic cells having double minute chromosomes or extrachromosomal DNA comprising the same steps as that of claim 1. Claim 30 is drawn to a method of identifying a therapeutic agent suitable for treatment of neoplastic cells comprising the same steps as that of claim 28.

Eckhardt et al teaches a method of determining micronucleation in response to hydroxyurea comprising determining the level of micronucleation (Table 2, page 6677). The test cells overexpress the Myc oncogene and Eckhardt et al teaches that hydroxyurea treatment leads

to loss of Myc and to differentiation of the tumor cells. Eckhardt does not expressly teach an assay method for identifying therapeutic agents. However, Snapka et al teaches that an approach to the problem of cancer cells which overexpress undesirable amplified genes is to look for ways to increase the probability of loss of the amplified genes and reports that cells grown in the presence of hydroxyurea have an increased rate of loss of DHFR genes. Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the methods of Eckhardt et al to make a method for identifying therapeutic agents which increase loss of extrachromosomal DNA or double minute chromosomes. One would have been motivated by the success of Eckhardt in demonstrating that hydroxyurea induces the loss of amplified Myc.

10. Claims 1, 3, 4, 28, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckhardt et al (Eckhardt, S.G. et al, Proc. Natl. Acad. Sci. USA, 91: 6674-6678, 1994; cited in the IDS) in view of Snapka et al (Snapka, R.M. et al, Proc. Natl. Acad. Sci., USA, 80: 7533-7537, 1983; cited in the IDS) and further in view of U.S. Patent 5,858,667 (Dertinger et al, supra).

The methods of claims 1, 3, 28, 29 and 30 are discussed above. Claim 4, dependent from claim 1, is limited in that the determination of micronuclei is done by FISH, flow cytometry, centrifugal centrifugation or histone GFP labeling. Neither of Eckhardt et al nor Snapka et al teaches methods of measuring micronuclei by FISH, flow cytometry, centrifugal centrifugation or histone GFP labeling. However, U.S. Patent 5,858,667 disclose a method of measuring

micronuclei with flow cytometry and teaches that this method is rapid, simple and accurate (column 2, lines 61-63). Thus, it would have been prima facie obvious to one of skill in the art at the time the invention was made to have used to the method of U.S. Patent 5,858,667 to modify the methods of Eckhardt et al to measure micronuclei formation.

11. Claims 1, 2, 28, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eckhardt et al (Eckhardt, S.G. et al, Proc. Natl. Acad. Sci. USA, 91: 6674-6678, 1994; cited in the IDS) in view of Snapka et al (Snapka, R.M. et al, Proc. Natl. Acad. Sci., USA, 80: 7533-7537, 1983; cited in the IDS) and further in view of Livingstone et al (Livingstone, L.R. et al, Cell, 70: 923-935, 1992; cited in the IDS).

The methods of claims 1, 28, 29 and 30 are discussed above. Claim 2, dependent from claim 1, is limited in that the test cells contain no functional tumor suppressor protein. Neither of Eckhardt et al nor Snapka et al teaches methods using cells without functional tumor suppressor protein. However, Livingstone et al teaches that alterations in the p53 leading to lack of a functional tumor suppressor protein may lead to gene amplification and that p53 mutations are present in a wide variety of cancers (page 923). Thus, it would have been prima facie obvious to one of skill in the art at the time the invention was made to have used to cells lacking a functional p53 tumor suppressor protein in a method to test for therapeutic compounds which increase micronuclei formation.

12. Claims 1, 3, 4 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimizu et al (Shimizu, N. et al, Nature Genetics, 12: 65-, 1996; cited in the IDS) in view of Snapka et al (Snapka, R.M. et al, Proc. Natl. Acad. Sci., USA, 80: 7533-7537, 1983; cited in the IDS).

Claims 1, 3 and 29 are discussed above. Claim 4, dependent from claim 1, is limited in that the determination of micronuclei is done by FISH, flow cytometry, centrifugal centrifugation or histone GFP labeling.

Shimizu et al teaches an assay for determining micronuclei formation using FISH where the test cells over express the Myc oncogene (see page 66, 2nd column, and page 67, Table 1). Shimizu et al also teaches that normal cells produce micronuclei at very low rates (page 68, 2nd column). Shimizu et al does not expressly teach a method for identifying therapeutic agents but suggest that elimination of double minute chromosomes from tumor cells would provide a chemotherapeutic strategy to target tumor cells. Snapka et al teaches that an approach to the problem of cancer cells which overexpress undesirable amplified genes is to look for ways to increase the probability of loss of the amplified genes. Thus, it would have been prima facie obvious to one of skill in the art to have used the methods of Shimizu et al to make a method for identifying therapeutic agents.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 3, 4 and 29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,033,849 in view of Snapka et al (supra).

Claims 1, 3 and 29 are discussed above. Claim 4, dependent from claim 1, is limited in that the determination of micronuclei is done by FISH, flow cytometry, centrifugal centrifugation or histone GFP labeling.

U.S. Patent 6,033,849 claims an assay for determining micronuclei formation using nucleic acid probes where the test cells over express various oncogenes. Snapka et al teaches that an approach to the problem of cancer cells which overexpress undesirable amplified genes is to look for ways to increase the probability of loss of the amplified genes. Thus, it would have been prima facie obvious to one of skill in the art to have used the methods of U.S. Patent 6.033,849 to make a method for identifying therapeutic agents.

14. Claims 1, 3, 4 and 29 are rejected under 35 U.S.C. 103(a) as being obvious over U.S. Patent 6,033,849.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by a showing of a date of invention for the instant application of any unclaimed subject matter prior to the effective U.S. filing date of the reference under 37 CFR 1.131.

U.S. Patent 6,033,849 claims an assay for determining micronuclei formation using nucleic acid probes where the test cells over express various oncogenes. Snapka et al teaches that an approach to the problem of cancer cells which overexpress undesirable amplified genes is to look for ways to increase the probability of loss of the amplified genes. Thus, it would have been prima facie obvious to one of skill in the art to have used the methods of U.S. Patent 6.033,849 to make a method for identifying therapeutic agents.

Conclusion

No claim is allowed. This rejection is not made final because of the new grounds of rejection.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
March 26, 2001

Brenda Brumback
BRENDA BRUMBACK
PATENT EXAMINER